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DISEASES OF THE NERVOUS SYSTEM

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

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DISEASES of the NERVOUS SYSTEM

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A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

*The Diagnostic Problem of Tumors at the Foramen Magnum.**

MARJORIE R. PIEHL, M.D., H. H. REESE, M.D. and H. F. STEELMAN, M.D.
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Meningiomas of the posterior fossa are of interest not only because of their relative rarity, but more particularly because of the differential diagnostic problems which they pose. Errors are especially common when the meningioma is located at or extends below the foramen magnum causing direct or indirect pressure on the upper cervical spinal cord, or when multiple tumors are present. The three cases reported here are included because they illustrate these diagnostic difficulties. Our experience with the first case, which was not diagnosed early enough to offer the benefit of neurosurgery, led us to review the problem and aided in a preoperative diagnosis of the succeeding cases.

The early diagnosis of meningiomas, which as a group comprise twelve to twenty per cent of all brain tumors[1] is especially significant because they are histologically benign and therefore, offer a good postoperative prognosis unless complicated by unusual vascularity, difficulties in the operative approach, or situations near vital centers. Their diagnosis in general is commonly aided by a history of unusually long duration of symptoms, varying of course with the site, and by roentgenological aid. Horrax[1] lists the following x-ray changes which are frequently associated with meningiomas: 1) "Erosion and vascularity"; 2) "Osteomatous changes"; 3) "Spikule-formation"; 4) "Diffuse thickening"; 5) "Enlargement of meningeal channels"; 6) "Calcification." Such roentgenological changes are significant if present, but they are frequently absent; bony changes may not be demonstrable particularly when the tumor is located at the foramen magnum.

The posterior fossa site is unusual, but has been reported with sufficient frequency and consistency of symptomatology to establish syndromes somewhat varying with the location within the posterior fossa. Campbell and Whitfield[2] reported nine posterior fossa meningiomas and classified them, exclusive of the foramen magnum site, into two main groups. One group included those arising from the under-surface of the tentorium, the lateral recesses and the posterior convexity. The symptomatology in this group so closely resembles cerebellar tumors that a preoperative differentiation is often impossible unless suggested by the unusually long duration of symptoms or the presence of typical calcification. In the other class are those meningiomas arising from the clivus or located in the cerebellar pontine angle. The diagnosis in these cases is again suggested by their slow growth and by the erosion of adjacent bony structures. The cranial nerve involvement closely simulates that caused by an acoustic neuroma. However, in two cases the differential diagnosis was aided by the fact that the vestibular response to caloric tests was not absent as would be anticipated in an acoustic neuroma.

Meningiomas located at the foramen magnum with which we are chiefly concerned in

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this report are relatively rare. Of 60 cases of meningiomas diagnosed at our University Hospital in the past ten years, only 3 have been located at this site of junction of the brain stem and the superior cervical cord. Tumors of this region fall into the spinocranial or craniospinal syndromes which are differentiated operatively or at autopsy on the basis of their site of origin, that is primarily in the upper cervical cord or in the posterior fossa with subsequent extension upward or downward through the foramen magnum. Cushing[3] has noted that the craniospinal types tend to arise from the basilar groove of the occipital bone and to lie anterior to the medulla and spinal cord, whereas the spinocranial tumors more commonly lie posteriorly or posterolaterally to the spinal cord, accounting for the frequent occurrence of pain in these cases. Clinically the differentiation may be impossible unless the course has been clearly one of cord signs and symptoms initially and only later cranial nerve or cerebellar signs develop. These latter signs may be manifested only as a slight nystagmus, facial weakness, slight tongue deviation or corneal hypesthesia as well as involvement of the 9th, 10th and 11th cranial nerves. The presence of occipital headaches preceding any cord signs may suggest a posterior fossa origin.

Because foramen magnum meningiomas are readily misdiagnosed as diseases not amenable to therapy such as amyotrophic lateral sclerosis, posterior lateral sclerosis, multiple sclerosis, and cervical spinal tumors, it is pertinent to review the salient points which if searched for, may lead to the correct diagnosis.

The craniospinal syndrome in brief as described by Bogorodinski[4] consists of "an onset characterized by suboccipital discomfort, protective rigidity of the cervical and occipital musculature, and sometimes pains or paresthesias of the shoulder girdle and upper extremity. At its maximum stage, the clinical symptoms are: 1) Paralysis of the extremities (hemiplegia, triplegia or tetraplegia). 2) Rigidity and pareses of the cervical muscles, abnormal posture of the head, or paresis of the 11th pair of cranial nerves. 3) Pains and paresthesias in the extremities and trunk. 4) Pains in the occiput and the neck. 5) Hemianesthesias or paranesthesias reaching up to the cervical dermatomes occasionally involving the skin field of the trigeminus. 6) Sphincteric disturbances. 7) Respiratory disturbances. 8) Horner's syndrome. 9) Cerebral symptoms such as paralysis of the 10th, 11th, 12th pairs of cranial nerves and choked discs are of infrequent occurrence."

Bogorodinski[4] also noted that although the course is slowly progressive, remission of isolated symptoms occasionally occurs. In discussing one of his cases Cushing[3] emphasizes the "diagnostic difficulties which were presented owing to the variability of the positive findings in the oft repeated neurological examination."

Our first case well illustrated also the variability of the subjective history. It has been noted by others that the complaint of occipital or nuchal pain may occur early in the course and may be absent or forgotten by the patient when he consults a physician. The pain is frequently aggravated in recumbency or on bending over. The weakness upon anterior flexion of the neck is also transient in some cases and suggests that in these instances the weakness may vary with the accumulative cerebrospinal fluid pressure in the cerebellomedullary cistern.

In a review of extramedullary tumors of the upper cervical region, in which they include spinocranial and craniospinal tumors, Saltz and Jervis[5] state that "in a survey of the cases of the literature, one is impressed by the infrequent notation of the appearance of *this* (diaphragmatic) involvement usually on the same side as the neoplasm." But when present this sign is of considerable diagnostic value. In one of our cases the diaphragmatic paralysis was homolateral to the tumor site and in the other it was contralateral. The above authors note that motor signs may be referable to both pyramidal tract and anterior horn involvement. They stress the frequent variability of sensory levels and false sensory levels in cervical lesions which they attribute to the degree of intraspinal pressure and the "tampon effect" of fluid above and below the tumor. Dissociation of pain and temperature from touch perception is not rare.

Elsberg and Strauss[6] record in their cases of spinal cord tumors with projection into the posterior fossa, the frequent complaint of subjective sensation of cold in the lower

extremities, and Cloward and Kepner[7] reported this complaint in their case of multiple meningiomas. Elsberg had noted this symptom only in cases of extra-medullary compression of the uppermost cervical segments.

Perhaps the most vivid impression one gains from reviewing the reported cases of meningiomas located at the foramen magnum is the lucidity of the clinical picture in retrospect, postoperative or postmortem, and the diagnostic pitfalls preceding such clarification. The errors appear to lie chiefly in failing to obtain an accurate history or in failing to attribute the proper significance to the subjective complaints obtained. Thus unless carefully questioned, the complaint of transient occipital or nuchal pain at the onset of the illness may not be elicited; the vague complaints of stiff neck or slight postural peculiarities may be underestimated; pains and paresthesias variable and transitory often seem to have no specific anatomical associations; the sensory disturbances are often bizarre as may be the motor disturbance suggesting scattered nervous system involvement.

Thus we feel justified in re-emphasizing that any patient complaining of occipital or nuchal pain or cervical weakness and stiffness with or without other neurological signs and symptoms deserves complete studies with the possibility of a foramen magnum neoplasm in mind. The same applies to all cases of the various neurosclerotic syndromes for which we have no specific diagnostic tests and may be confused with a neoplasm.

Diagnostic procedures such as lumbar punctures, oil myelograms and pneumoencephalograms which may disturb the dynamic adjustment of a space filling lesion in the posterior fossa or upper cervical cord are not without danger. They may precipitate marked exacerbation of symptoms or even death as is exemplified by the first of our cases, whose death was no doubt hastened by a cisternal pneumoencephalogram. Lumbar pneumoencephalograms were well tolerated in the other two cases and aided materially in substantiating the diagnosis. The ventricles may be of normal size or the entire system may be enlarged depending upon the degree of block. The most significant features are revealed in lateral views showing the fourth ventricle to be displaced forward or backward depending upon whether the tumor lies anteriorly or posteriorly to the medulla. That these changes may be minimal and their significance not appreciated is illustrated in our cases in which it was necessary for the roentgenological interpretation to be made in correlation with the clinical picture and thus appropriately evaluated (Figure 1).

Figure 1: Case No. 2: W.B. Pneumoencephalogram showing elevation and posterior displacement of the floor of the fourth ventricle consistent with a tumor occupying the region along the anterior borders of the foramen magnum. The fourth ventricle is outlined with stippling. Arrow points to its elevated and posteriorly displaced caudal portion. (Hyperostosis frontalis interna of no clinical significance.)

Our first case of a meningioma arising at the level of the foramen magnum illustrated a far advanced symptomatology which only in retrospect and in the light of the autopsy findings was seen to represent a typical case of the craniospinal syndrome. The second case presented many clinical features similar to case No. 1 and was correctly diagnosed preoperatively. Case No. 3 has been tentatively diagnosed as a meningioma at the foramen magnum; but because of the paucity of objective neurological changes and the subsidence of symptoms surgery has been deferred and the patient maintained under observation.

Case No. 1: E.P., 42 year old white female, first admission on August 25, 1948. History was somewhat unreliable with different accounts of the sequence and severity of symptoms. Initial chief complaint: weakness of the right arm and leg. Patient was well until

December 1947 when she had one or two dizzy spells weekly particularly on bending over, preceded by scotomata. She would fall to the ground with a generalized sensation of weakness and buzzing in the head. There were no convulsive movements nor loss of consciousness. After a few minutes she would be able to get up and resume her activities. She had injured herself several times in such falls. Headaches had been present for 22 years but in the last three months they had become severe and constant, beginning in the parietal and radiating to the occipital regions, associated with a tic of the right upper eyelid. December 1947, numbness and tingling in the fingers of the hand, at times with a complete loss of sensation; she would drop things from the left hand. May 1948, heaviness of the right arm and leg and pain radiating vaguely from the hip to the knee. Tingling, numbness and later weakness with inability to move the arm progressed until July 1948, when she lost all active motion in the right arm. Since August 18, 1948 completely bedridden with weakness of all extremities. Other significant complaints: occasional dyspnea, arrhythmia, swelling of the right foot, and severe anorexia. The patient had subsisted chiefly on a beer diet. Past medical history revealed laparotomy for a left ovarian tumor.

This obese patient was alert, cooperative and apparently free from pain. No abnormalities of the skull, but a slight tenderness of the posterior upper cervical region. Blood pressure 118/80, the heart equivocally enlarged. Slight edema of the right foot and ankle.

Neurological examination: cranial nerves intact with normal pupils, extra ocular muscles, visual fields and fundi. Right flaccid hemiparesis with exaggerated reflexes more marked on the right and with a transient positive Babinski; abortive ankle clonus bilaterally. Hoffmann reflex present bilaterally; abdominal reflexes absent. Sensory perception normal to all modalities except for variable impairment of the vibratory sense over the lower legs. Astereognosis was also variable. Slight dysmetria of the left upper extremity. There was slight weakness of the flexors and extensors of the neck. It is pertinent to note here that not only did the patient's complaints and history vary markedly from day to day, but also the neurological findings showed variation with considerable return of strength in the paretic extremities. Previous to completion of the laboratory studies such impressions as multiple sclerosis, hysteria and brain tumor were considered.

Laboratory studies: skull x-rays normal; x-rays of the chest revealed the right diaphragm to be slightly elevated above the left and a calcified primary complex in the right lung. Electroencephalogram normal. Lumbar puncture: August 26, 1948, initial pressure 180; clear fluid, no cells, protein 105, Wassermann negative, gold sol 0122221000. Lumbar puncture: (August 30, 1948) clear fluid, 6 cells, protein 100, Wassermann negative, gold sol 1233210000. The patient returned home for a brief stay, but because of the protein elevation was discharged September 22, 1948 as a brain tumor suspect.

Readmission for re-evaluation (November 17, 1948). She stated that she felt much better since her discharge and that the previous numbness and tingling in the extremities was no longer present, that she no longer had any headaches or dizziness "following the lumbar punctures." The weakness of the right extremities persisted with pain in the right shoulder. Complaints: early satiety, anorexia and constipation.

Physical examination was essentially the same as previously except for some increase of the edema in the right arm and hand but minimal in the pretibial areas bilaterally, right greater than left. Blood pressure 100/80, heart normal.

Neurological examination revealed marked weakness of the neck muscles with the patient unable to lift her head off the pillow; weakness of the extensor neck muscles although rotation laterally was fairly good. Tendency to nuchal rigidity but without any pain or true Brudzinski sign. Cranial nerves intact, no evidence of papilledema. There was almost complete right flaccid hemiparesis. The left extremities were paretic, but she was able to perform almost full range movements. Occasional brief involuntary jerkings of the right leg. Unsustained ankle clonus on the left and marked sustained ankle clonus on the right. The tendon reflexes 3 plus on the left, 4 plus on the right. Abdominal reflexes absent. Hoffmann present bilaterally, Bab-

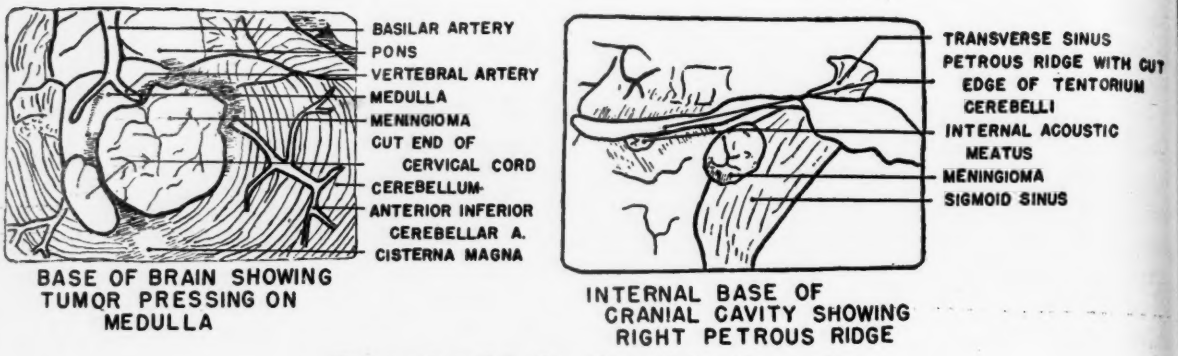
inski signs were inconstantly present bilaterally. Sensory examination normal to all modalities except for questionably impaired vibratory sensation from the iliac crest distally and marked dysstereognosis. The finger-to-nose test was fairly well performed on the left, heel-to-knee was poorly performed. Affect reaction euphoric. The respiratory excursions suggested intercostal and diaphragmatic impairment without respiratory embarrassment or use of accessory muscles.

Laboratory studies: Electroencephalogram normal; electrocardiogram nonspecific changes probably on a toxic basis. X-rays of the cervical spine normal. Stereo skull films: normal. Chest x-rays right diaphragm continued to be elevated with minimal compression atelectasis at the extreme base. The clinical impression at this time was a high cervical cord tumor. On November 24, 1948 a cisternal puncture was done and revealed slightly bloody fluid with negative pressure. A lumbar puncture simultaneously at L4 revealed clear fluid under initial pressure of 130 which rose and fell slowly upon jugular compression to 160. Injections of 10 cc. of air increased definitely the outflow from the cisternal puncture needle and the reverse was obtained with the same results suggesting free communication between the lumbar to cisternal needles. Spinal fluid protein of 80 milligrams, 3 cells, negative Wassermann and gold sol 1233210000. On December 2, 1948 urinary retention necessitating indwelling catheter. On December 7, 1948 a pneumoencephalogram was done by the cisternal route (inability to sit up). Fifty-eight cc. of clear spinal fluid were removed and 55 cc. of air injected. The patient's condition remained very satisfactory throughout the procedure. The pneumoencephalogram films were reported as follows: "The 4th ventricle is visualized in the lateral films and is of normal size and shape. There is no gas in the ventricular system above this point. There is only a small amount of gas in the subarachnoid space and this is present only on the left side and chiefly in and along the Sylvian fissure. The amount of visualization is inadequate for diagnosis."

The patient was given the routine post-pneumoencephalogram therapy which at this hospital consists of oxygen at 6 liters per minute, 1,000 cc. of intravenous fluids which were administered over a 3 hour period. The patient's blood pressure, respirations, temperature remained normal but tachycardia of 120 persisted and therefore oxygen was continued. The next morning (December 8, 1948) the patient's condition was considered satisfactory except for a slight lethargy. The patient became pale and slightly cyanotic during the day. She was very lethargic with the skin hot and moist. Blood pressure was 124/60, temperature 101 rectally, pulse 112, respirations 24. The respirations were regular but very jerky with chiefly abdominal breathing and with poor thoracic excursions. Inability to cough or clear the throat. The pupils were miotic with questionable reaction to light. There appeared to be a bilateral abducens paresis. The voice was very weak. Tracheal bronchial aspiration was done immediately with marked improvement. The neuro-surgery consultant (Dr. T. C. Erickson) recommended an oilmyelogram during which procedure it was necessary to intubate the patient and administer oxygen by mask. No encroachment on the oil silhouette up to the first cervical vertebra; the oil passed readily into the basal cisterns and a complete block was not present. The cerebrospinal fluid pressure at this time was 420. The patient rapidly became comatose with impaired respiration. A ventricular puncture was done with the removal of 6 cc. of fluid and injection of 12 cc. of air. The ventriculogram was reported as an essentially normal ventricular system with no evidence of an intracranial space occupying mass. The patient expired on December 9, 1948.

The post mortem findings outside the central nervous system were a confluent bronchopneumonia, pulmonary congestion and edema, cardiac dilatation, numerous ulcers (1 mm. in diameter) over the entire gastric mucosa and a recent hemorrhage from an erosion of the duodenum.

The gross brain examination was as follows: There was a small amount of blood at the site of needle puncture in subarachnoid membrane covering the cisterna magna. There was no herniation of cerebellar tonsils. A gray, somewhat lobulated mass, measuring 4 cm. in diameter, was seen growing from the dura of the left anterolateral wall of the posterior fossa just above the rim of the foramen magnum. It had flattened the



Figures 2 and 3: Drawings giving the anatomical relationships of tumors in case of multiple meningiomas. Case No. 1, E.P.

medulla and displaced the 4th ventricle backward and to the left. A second tumor, 2 cm. in diameter, was present on the right sphenoidal ridge (Figures 2 and 3).

Microscopic sections were taken through the tumor, medulla, upper cervical cord, lower cervical cord, thoracic cord and lumbar cord and stained with hematoxylin and eosin, Weil's method for myelin and the Swank-Davenport modification of the Marchi stain for degenerating myelin.

The microscopic findings are as follows:

Tumor: The architecture consisted of whorls and alveolar masses of lilac staining meningothelial cells separating, and mixed with, eosinophilically staining capillaries and collagenous connective tissue. The capillaries had thick, hyaline walls with several layers of fibrocytes. In some the lumina were occluded by the proliferating cells, while a few contained fresh red blood cells. A few psammoma bodies were present, varying in size from the diameter of a red blood cell to the diameter of a small artery. Their concentric rings stained various colors, from deep purple to pinkish-lilac, and surrounding the psammoma bodies were one or two rings of pink hyaline material with an occasional fibroblast nucleus (Figure 4).

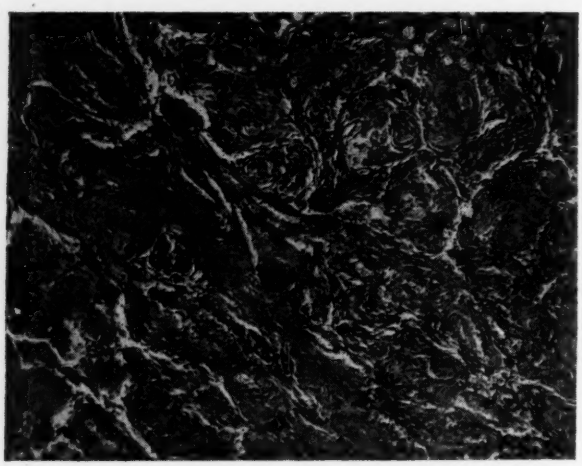
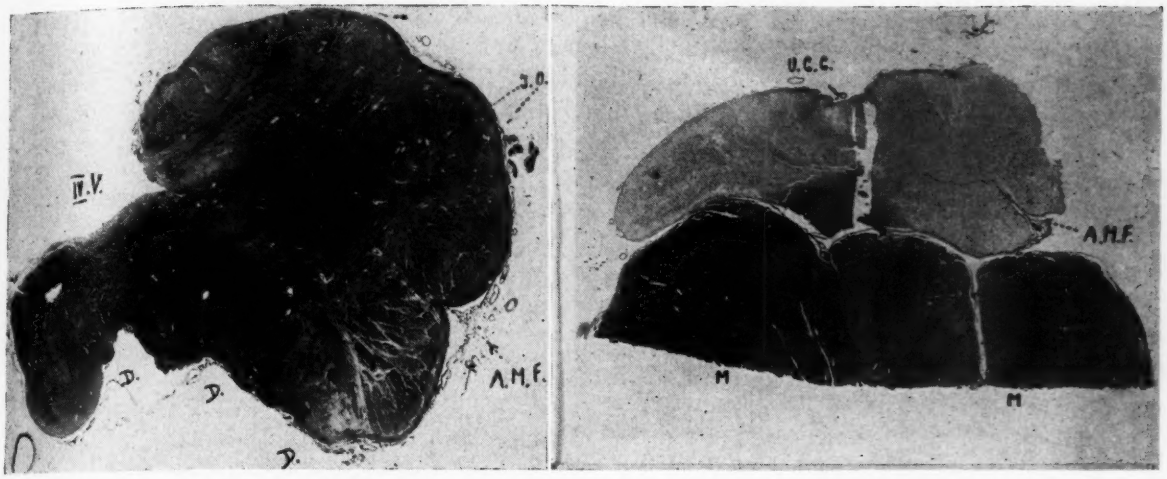


Figure 4, Case No. 1: E.P. Section of meningioma, H. & E. Stain. The fibroblastic structure with whorl formation and with a psammoma body in the center of the section is characteristic.

Medulla: The defect caused by the tumor was clearly evident and the medial longitudinal fasciculus, medial lemniscus and tectospinal tracts were bowed with the convexity to the opposite side. The olives were present on both sides in the most rostral sections. The cells of the right reticular formation showed chromatolysis with eccentric nuclei and clumping of the Nissl substance at the nuclear membrane. On the side of the tumor the cells of the reticular formation showed a more severe degree of chromatolysis with shrinking of the cell body and a more pyknotic staining reaction. The wedge of tumor tissue drove into the medulla at the region of the spinal fifth nucleus and separated the cuneate nucleus posteriorly from the ambiguous nucleus and the inferior olive anteriorly, in respective walls of the depression. The cells of the hypoglossal nucleus and the dorsal motor nucleus of the vagus on both sides were shrunken and showed chromatolysis. In this region bilaterally, there was demyelinization, capillary congestion, and ring-like hemorrhages, with red blood cells free in the tissues. The cells of the cuneate nuclei showed various degrees of disintegration ranging from severe chromatolysis to ghost cells. Demyelinization was particularly severe on the left external surface just inferior to the olive, and in the floor of the fourth ventricle. The olivary cells appeared abnormal also. The olive on the right side



Figures 5 and 6: Two sections from medulla[5] at level of inferior olive to junction with upper cervical cord[6] showing defect caused by the tumor. Case No. 1, E.P.

IV. V. = 4th ventricle
I. O. = Inferior olives
A. M. F. = Anterior Median Fissure
D. = Defect compression by tumor
M. = Meningioma
U. C. C. = Upper Cervical Cord

has been completely destroyed in the most caudal sections. Congestion of the capillaries was prominent especially on the left side where there was some extravasation of red blood cells. There was extensive demyelinization of scattered portions of the tissues especially next to the tumor in the region of the spinal fifth nucleus, as well as in the midline structures of the dorsal half of the section (Figures 4 and 5).

Upper Cervical Cord: There is a moderate amount of intensely eosinophilically staining collagen in the subarachnoid space and in the adventitia of the small intramedullary blood vessels with a minimal amount of perivascular demyelinization in the anterior horns. The cells of the central canals have proliferated extensively. The anterior horn cells stain darkly and are slightly shrunken. There are a few places in the anterior horns where small ring hemorrhages occur. The myelin stain shows a minimal demyelinization of the gracilis and cuneate columns and of the periphery of one of the lateral funiculi and to an even lesser extent in the column of the opposite side. Swank Davenport stain: the posterior columns are very pale and have taken little of the stain, the gracilis tract being less stained than the cuneate. One of the lateral columns shows extensive staining and both the anterior funiculi show much degenerating myelin.

Lower Cervical Cord: The H & E section here shows similar changes to those described for the upper cervical region. The Swank Davenport showed very slight staining of the lateral corticospinal and the gracilis tracts, while the spinocerebellar tracts and the anterior funiculi took up a great deal of the stain. The anterior and posterior roots both had tubes of degenerating myelin, irregularly scattered through them. The fat of the anterior horn cells took the stain.

Thoracic Cord: The perivascular and subarachnoid collagen here again was increased and the cells of the central canal were markedly proliferated. There was some perivascular demyelinization around the blood vessels in the grey horns. The anterior and posterior horn cells were shrunken and more

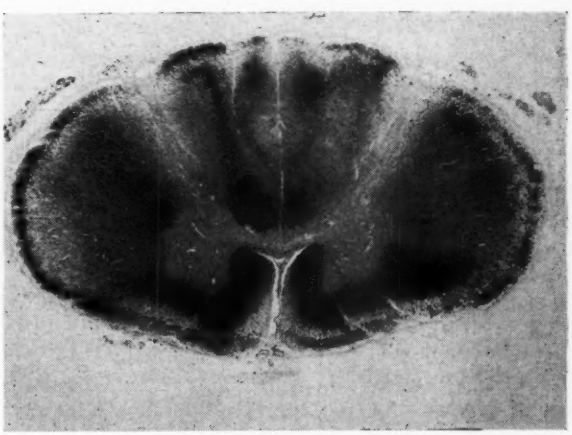


Figure 7: Upper thoracic cord. Swank-Davenport stain for degenerating myelin, showing degeneration concentrated in posterior and anterior columns.

darkly staining then normal. The myelin stain showed no appreciable demyelinization of the white tracts except for the superficial portions of the lateral funiculi (Figure 7).

Lower Thoracic Cord: The H & E stain showed changes described elsewhere for H & E stained cord sections. Some of the cells show chromatolysis in addition to being shrunken. The Swank Davenport stain showed degenerating myelin around the periphery of the cord and in the anterior funiculi. One of the lateral columns showed some involvement.

Lumbar Cord: The myelin sheaths of the anterior funiculi were disorganized in appearance. The peripheral portions of the cord were stained more lightly than normal. The posterior roots were demyelinated to a severe degree on one side.

Following the autopsy diagnosis, the x-ray films were reviewed and then reported as showing slight forward displacement of the lower portion of the fourth ventricle. In the myelogram films there was a rather sharp cut off to a small portion of the oil shadow at the level of the foramen magnum. These were the only findings which could be considered positive and suggestive of a lesion at the level of the foramen magnum.

It is significant to point out that the case history as given above was abstracted from the numerous histories obtained from this patient during the course of her two hospital admissions. After knowing the autopsy findings in this case it is believed that the symptoms and their sequence as given represent the true clinical course. But it is also pertinent to report the inconsistencies in the history which "muddied the waters" as frequently occurs on repeated questioning which is intended to clarify the picture. The patient originally complained of headaches of recent severity, she later denied that these had altered in 22 years; the paresthesias were at one time attributed to an electric shock from faulty wiring in a refrigerator; the headaches disappeared completely over a two and one-half month period following two lumbar punctures at which only 10 cc. of fluid are routinely removed. The right hemiparesis subsided almost completely on one occasion following an injection of prostigmine. Thus the diagnoses entertained at various times during the course of her illness ranged from "hysteria to multiple sclerosis, amyotrophic lateral sclerosis and a high cervical cord neoplasm."

The above case is also of interest in that the presence of two meningiomas (in a patient with no stigma of Von Recklinghausen's disease) places it in the classification of multiple meningiomas as defined by Cushing and Baily thus meeting the strict limitations of this diagnosis when distinguished from Von Recklinghausen's disease and the groups classified as meningiomatosis with diffuse and coalescing neoplastic nodules. Echols[8] in 1941 found only 52 reported cases of multiple meningiomas and within that number the validity of the diagnosis was questionable in some of the cases.

Case No. 2: W.B., a 52 year old white female seen in the out-patient department on November 11, 1948 and hospitalized on December 14, 1948 for diagnostic evaluation.

Chief complaints: Pain in back of neck and occiput for two years and weakness of the right arm for seven months.

The nuchal pain was a feeling of tightness in the posterior cervical region on the right with the pain radiating to the temple and behind the right ear, also a tight band-like and occasional sharp stabbing frontal headache. Headaches had progressed until they occurred daily with more severity in the morning. Seven months preceding admission the sense of touch had diminished in the fingertips on the right. Tingling paresthesias soon developed and the hands (not the legs) felt cold. A few weeks later onset of weakness of the right hand with a tendency to drop objects from the hand. The weakness progressed up to the right shoulder and the shoulder became painful. Intention tremor with fatigue developed. There was a vague sensation of numbness across the abdomen. A few weeks preceding admission she noticed ataxia and weakness of both legs and occasional sharp pain along the left thigh to the knee; pain and stiffness in the left shoulder and a constricting band sensation around her neck increased.

Other complaints were slight blurring of vision, O.D.; urinary urgency, frequency and nocturia.

Social history was significant for considerable emotional disturbance.

Neurological findings varied but were es-

sentially as follows: Patient was obese, alert, cooperative and did not appear ill. Blood pressure 134/86. Temperature, pulse and respiration normal. The gait was described as bizarre. Cranial nerves were intact except that one examiner reported ptosis of the right eyelid said to be present for the past five to six years. Questionable increase of muscle tone in the right arm and moderate weakness of all muscle groups in the right upper extremity and associated ataxia. Tendon reflexes were hyperactive but equal bilaterally; no pathological reflexes. Skin of the right hand was more dry, scaly, and colder than the left and later became edematous. A vague sensory level was present at the right elbow and shoulder.

Skull x-rays were negative except for marked hyperostosis frontalis interna. X-rays of the cervical spine revealed considerable sclerosis and spurring of the cervical joints, representing degenerative joint disease. Electroencephalogram showed high voltage 1½ to 3 per second waves in all leads; localization varied but suggested a left central or occipital lesion.

It was believed that the hyperostosis frontalis interna and the cervical degenerative arthritis might account for most of the patient's complaints, but the general diagnostic impression was probable conversion hysteria. A pneumoencephalogram was done on December 20, 1948 to rule out cerebral lesion. Cerebrospinal fluid pressure at that time was 50 mm. of mercury in the sitting position. Cerebrospinal fluid 50 mgms. protein, no cells, Wassermann negative, gold sol 1222100000. X-rays showed all of the ventricles to be within the upper limits of normal in size. The basal cisterns were slightly enlarged, a few distinct arachnoid channels were present in the right parietal region. There was some downward displacement of the anterior horns of the lateral ventricles apparently secondary to the thickened frontal bone tables. The patient was somewhat lethargic the following day, and there were signs of pulmonary congestion. Chest x-rays showed the right diaphragm to be elevated 2 interspaces with partial atelectasis in the right middle and lower lobes. The following day a superimposed bronchopneumonia was noted.

The patient became confused and emotionally liabile. Neuropsychiatric consultation on January 3, 1949 revealed right hemiparesis with hypertonicity and dyscoordination of the right leg, a questionable right Babinski and abortive ankle clonus on the right. Weakness of the flexors, extensors and rotators of the neck. Patient tended to fall to the right upon sitting up. Horizontal mystagmus on left lateral gaze. Sensory impairment of the right arm was vague as previously reported. Clinical impression: Foramen magnum meningioma on the right. The pneumoencephalogram films were reviewed with this in mind and reported as showing: Definite elevation and posterior displacement of the floor of the fourth ventricle. The ventricles are of normal size. The displacement of the fourth ventricle is consistent with a mass occupying the region along the anterior margin of the foramen magnum (Figure 1).

On January 6, 1949 a suboccipital craniotomy revealed that the upper cervical cord and lower medulla were markedly displaced from right to left by an encapsulated tumor 5 x 3 cm. in size. The spinal accessory nerve ran over the surface of this tumor. The upper cervical nerve roots were displaced downward by the tumor and the 9th, 10th and 12th cranial nerves were displaced upward. The vertebral artery was displaced upward and compressed by the tumor. Attachment of the tumor was to the anterior portion of the foramen magnum on the right side. The tumor was removed completely. Microscopic sections showed many groups of tumor cells separated by irregular fibrous tissue septa. The tumor cells were generally slightly elongated and similar in appearance. They appeared granular with slightly vacuolated cytoplasm. Nuclei were equal in size and marked by fine particles of chromatin. There were no mitotic figures. Impression: Meningioma, mesotheliomatous type.

The patient's postoperative course was stormy with respiratory embarrassment and she expired the day following surgery. No autopsy was obtained.

Case No. 3: V.K. This case has been diagnosed clinically as a tumor, probably meningioma, just above the foramen magnum. This diagnosis has not been verified as yet by surgery. V.K. entered the hospital on February 24, 1949 and was discharged on March 6, 1949. The patient had numbness and tingling of both hands for one week in 1948. In

January 1949, recurrences of paresthesias of both hands similar to previous experience, however, in addition numbness and weakness of the legs from "the knees to waist" of approximately two weeks' duration were present. Preceding admission she complained of intermittent pain behind the left ear. A day after the onset of this left head pain she noticed weakness of the left leg and limped for approximately one week and developed paresthesias of the fourth and fifth fingers of the left hand with weakness of that hand. She was able to continue working until five days preceding admission. The only residual complaint at the time of admission was the intermittent pain behind the left ear. Past medical history, a "nervous breakdown" four years ago characterized by headaches, confusion and hallucinations.

Neurological examination revealed the head and neck to be normal. Cranial nerves were essentially intact except for deep cupping of the optic discs, more marked on the left and with a myopic opto-kinetic nystagmus. The motor system revealed normal tonus and strength throughout and no reflex changes other than absent abdominals (probably caused by obesity). Sensory examination was normal throughout. No cerebellar signs. Lumbar puncture showed an initial pressure of 230 with active fluid dynamics. The fluid showed 3 cells, a protein of 22, gold sol 0000000000 and Wassermann negative. The x-ray of the skull showed the calcified pineal in the midline but lateral views suggested the upper limits of normal in position of the pineal body. No bony abnormalities. A pneumoencephalogram showed the ventricles to be slightly to moderately enlarged without deformity or displacement from the midline. The lateral views revealed a forward displacement of the fourth ventricle and the distance of its floor from the dorsum sella was below normal. The procedure was well tolerated except for a moderate bradycardia. On the basis of the history and the pneumoencephalogram findings, a diagnosis of meningioma just above the foramen magnum was made, despite the absence of positive objective neurological disturbances.

In consultation with the Neurosurgery Department and discussion with the patient and her family, it was felt that suboccipital craniotomy with exploration could be deferred after a period of observation.

In the absence of clinical evidence for multiple sclerosis, metabolic or dyscrasic cord diseases or for a psychoneurotic disorder, the anterior displacement of the fourth ventricle is of great clinical significance in view of the subjective complaints. The posterior foramen magnum meningiomas produce pain, paresthesias and fleeting posterior fossa symptoms all caused by dynamic cerebrospinal fluid pressure alterations as seen in hygromas.

Summary

1) The clinical syndromes presented by tumors located at the level of the foramen magnum have been reviewed.

2) The diagnostic procedures and the problems of differential diagnosis are emphasized.

3) Three cases are presented.

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Artane in the Treatment of Parkinsonism

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On account of the chronic nature of the disease and the severe progressive disability associated with Parkinsonism, the quest for new drugs to bring relief is unending.

For the past six months a series of twelve patients with either arteriosclerotic or post-encephalitic Parkinson's disease have been treated with a new antispasmodic, Artane Trihexyphenidyl. Two of these patients were not under my immediate supervision but were supplied with Artane and are included in this series through reports from the family physicians.

Artane Trihexyphenidyl is a synthetic compound similar in chemical composition to atropine but its effect in reducing sialorrhea is not as extensive as that occurring with some of the other belladonna alkaloids. In treating most of these patients their previous medication was considerably reduced or eliminated although Artane was tolerated well in combination with others of the belladonna group.

In order to work out some way to evaluate improvement the following data were obtained for each patient:

1. Subjective report of patient.
2. Report of relative.
3. Appearance and posture.
4. Performance in daily life.
5. Neurological examination.
6. Movement rate and gait.

The neurological findings were graded from one to four on the basis of severity.

Post-Encephalitic Group

The results in patients with post-encephalitic Parkinson's syndrome were as follows:

Improvement:

Decided (EM., E.N., H.R.)	3
Slight (C.I., E.W.)	2
None (C.H.)	1

Patient E.N. who was unable to dress himself before taking Artane could subsequently dress himself. He formerly did not eat breakfast because of intense tremor which was reduced by Artane and he was able to eat and feed himself at breakfast.

Patient E.M. had an approximate 25 per cent reduction in tremor and rapid alternating movements which were impossible before taking Artane became normal on the left and improved on the right. When she ran out of Artane in May after being on it for two months, gait slowed up, severe tremor became manifest on the right, and rapid alternating movements again became defective. When put on Artane again there was approximately 50 per cent less tremor in the right hand and 25 per cent improvement in rapid alternating movements on the right.

Patient E.W. who showed slight improvement at first after the dose of Artane was increased had an approximate 25 per cent improvement in rapid alternating movements on the right and an approximate 50 per cent improvement in rapid alternating movements on the left.

Patient C.I. reported that Artane was the best drug he had ever taken in twenty-five years of treatment. Restlessness which was one of his major complaints had been markedly decreased.

Arteriosclerotic Group

The results with six patients with arteriosclerotic Parkinson's disease were as follows:

Improvement:

Slight (S.S., O.B., E.C., J.P.)	4
None (C.J., C.M.)	2

One, E.C., reported improvement four times of the six times he was seen. Tremor in the hands was improved approximately 25 per cent and rapid alternating movements were improved 25 per cent.

Regarding the two patients with arteriosclerotic Parkinson's disease followed by their family physician, one physician[1] reported: "The patient definitely feels that of all the drugs she has taken (Tincture of Belladonna, Scopolamine, Stramonium, Vinobel, and Benadryl), Artane, which she has used since March 1949, has been the most satisfactory."

The other[2] reported: "There seemed to be a rather prompt and persistent relief of the backache which might be considered relief of muscle spasm. . . . There may have been some slight relief of spasticity."

Use With Other Drugs

After taking Artane for several months four patients had Tolserol (Myanesin) added to their usual regime. Tolserol has a curare-like effect and has been advocated for relaxation of muscle spasm in Parkinsonism by Berger and Schwartz[3] and Gammon and Churchill.[4] In no case did Tolserol bring about improvement or alter the previous benefit which had been obtained from the use of Artane.

Artane along with Benadryl[5] three or four times a day, seemed to bring about maximum improvement in patients E.M., H.R., J.P.

Dosage

Artane is available in 2 and 5 mg. tablets. At first 2 mg. doses were used three times a day at meal time but they were ineffectual in most instances. Artane is now initially prescribed in 5 mg. doses three times a day with meals. An additional dose may be taken at bedtime and the dosage may be increased gradually so that some patients may take as much as 10 mg. three times a day.

On the basis of an article on Parkinsonism in a series in The Lancet called Disabilities,[6] it was deemed advisable to administer larger doses of antispasmodic alkaloids in the morning rather than late in the day so that the patient would have maximum relaxation during that part of the day calling for greater activity. For that reason should it be necessary to increase the dosage of Artane, it is best done by additions first at breakfast and then at lunch.

Precautions

Reactions were few but there were some: dizziness, staggering, and drowsiness. In one patient, E.C., with 18 mg. of Artane daily, disorientation and irresponsible behaviour appeared, and in another patient, C.I., confusion. These symptoms disappeared when the dosage of Artane was reduced.

Artane is not contraindicated in the presence of circulatory, hepatic, or renal disorders. Blurred vision occurred in only one of these patients and then was relieved by reducing the dosage. Artane is devoid of severe acute side reactions, and side reactions are infrequent as compared with other drugs used for Parkinsonism.

The findings in this series are in general similar to those reported by Corbin[7] of the Mayo Clinic who treated over seventy cases with Artane. They also agree with the findings in a series of one hundred and seventeen cases reported by Doshay and Constable[8] at the Vanderbilt Clinic, New York City.

Summary

Of six patients with post-encephalitic Parkinson's syndrome treated with Artane three showed decided improvement, two showed slight improvement and one showed no improvement.

Of six patients with arteriosclerotic Parkinson's disease treated with Artane four showed slight improvement and two showed no improvement.

Author's Note: Artane was furnished through the courtesy of Dr. Guy W. Clark of Lederle Laboratories Division of the American Cyanamid Company. Tolserol was furnished through the courtesy of Mr. John Parr, E. R. Squibb and Sons Company.

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The Technique of Cistern Puncture

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As a means of obtaining cerebrospinal fluid for routine examination, cistern puncture has the advantages of being simple, relatively painless, and quite free from the disagreeable after-effects which so frequently follow lumbar puncture. It lends itself to office or clinic procedure on ambulatory patients. The chief reason that it is not more widely adopted is the fear of trespassing upon important structures close to the medulla.

Ontaneda,[1] in a review of the literature, found 30 deaths among 50,000 cistern punctures. Five of these were due to puncture of brain stem or arteries, displaced by tumors. Two were due to block of the cistern, in cases of increased intracranial pressure, one to laceration of the posterior cerebellar artery, and the remaining 22 were due to traumatism of the brain stem, with resulting hemorrhage. In his own series of 4,500 punctures, there were no deaths, while in the competent hands of Lange,[2] Pedersen,[3] and Voss,[4] with a total of more than 20,000 cases of cistern puncture, there were no fatalities. Klinke had two fatalities in 10,000 cases of cistern puncture, and two fatalities in 2,000 cases of lumbar puncture, all of them associated with increased intracranial pressure and block in the cistern.

In an effort to diminish these hazards, two procedures have been devised to estimate the depth to which the needle will penetrate the dura. The first is based upon an estimate of the depth of the cistern from its relation with the mastoid process; and the second, a more direct method, by which the needle is pointed first at the base of the occiput and then worked into the cistern. The second method has the undesirable feature in that it is somewhat more painful and, because, by pressing the needle against the occiput, the point may be blunted or the needle bent. In addition, puncture of one of the epidural veins is not infrequent, so that a bloody tap results.

The mastoid process was used as reference point by Letnik and Faidel[5] and by Pires.[6] Ontaneda,[1] measuring 100 crania, found the distance from the mastoid to the posterior border of the foramen magnum to vary between 25 and 30 mm. in 93 per cent of cases. In other words, the distance from the nape of the neck to the point of the mastoid process is 20 mm. farther than the distance of the cistern in man, and 17 mm. farther than it is in women. He recommends that the needle never be inserted more than 3 cm. beyond the calculated depth of the cistern, and he recommends a slight downward angulation of the needle, so that if the point does touch the nervous system, it will be the upper end of the spinal cord rather than the medulla. We have reviewed the work of these and of other authors in order to increase the precision of this useful method of cistern puncture.

Craiometric Studies

Since the mastoid process is somewhat variable in size and height and sometimes asymmetrical, we choose the highest point of the posterior border of the process. Although there is considerable variation, the use of this posterior mastoid point has the advantage of being always on the same horizontal plane as the cistern, thereby avoiding errors through the variable height of the mastoid process. This study was carried out in 200 crania.

In 20 cadavers we also found such variability and such frequent penetration on the spinal cord or the medulla that we sought a method of keeping the needle in the proper line without going too deeply. The point of insertion of the needle must be chosen so that the needle will follow the shortest possible course to the cistern, although if the needle is pointed in an upward direction, there is slightly more space between the dura and the nervous structure. It stands to reason that there should be no lateral deviation or rotation of the head during cistern puncture, as rotation or lateral deviation of the head interferes with the maintenance of proper relationships.

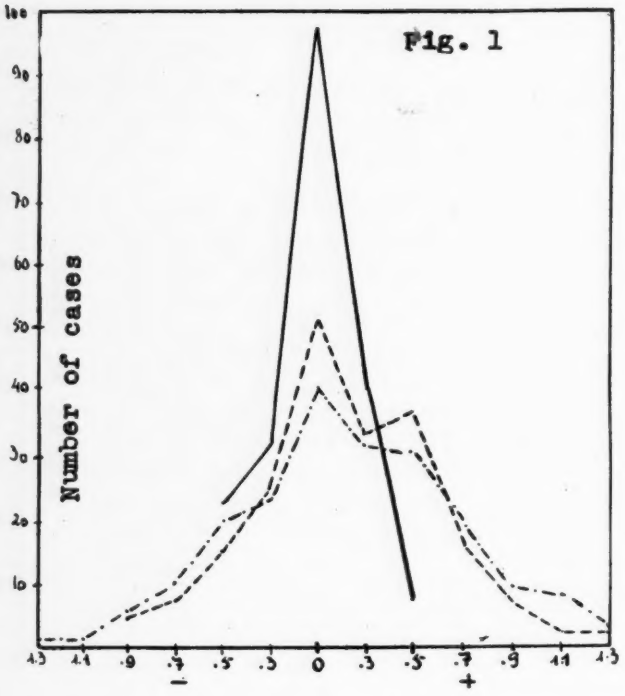

Fig. 1

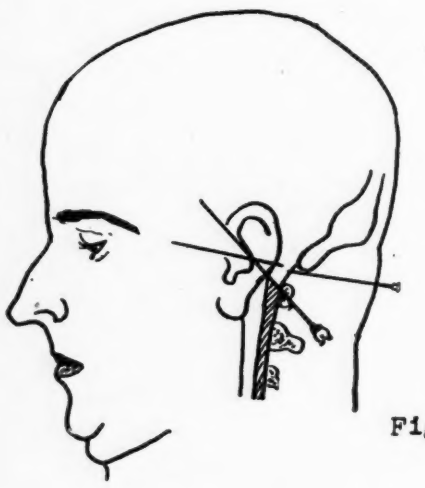

Fig. 2

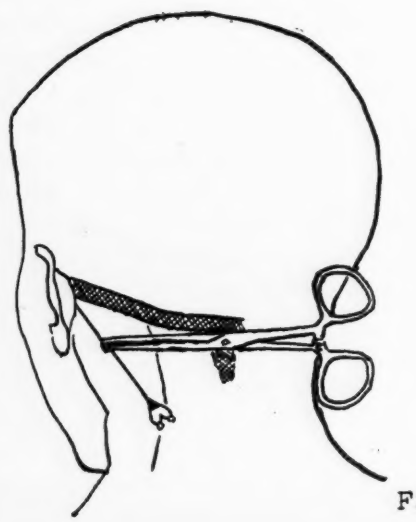

Fig. 3

Clinical Studies

When the mastoid reference points were used, the error of calculation was less than 1 cm. Using the flexion axis of the head reduced this to +0.5 cm., which is somewhat safer, because the free space in the cistern at the level of the puncture is adequate (Fig. 1). In order to determine the flexion axis of the head, a line is drawn on the skin from the lateral margin of the orbit to the base of the mastoid process and an applicator is placed parallel with this line, while the patient bends and extends his head. The point of intersection of these lines corresponds to the flexion axis of the head (Fig. 2). The point of intersection of the needle is in the sub-occipital triangle, close to the flexion axis of the head. We prefer to have the head in complete flexion. This allows more precise measurement, enlarges the atlanto-occipital space, and stretches the dura and the atlanto-occipital membrane and makes the penetration of the instrument more easily palpable. A mark is placed on the needle 5 mm. above the expected depth of the cistern, so that the instrument will not be thrust in too far, and with the stylet and forceps placed as shown in Figure 3, the point of the needle is inserted through the skin and brought forward along the stated line to a depth of 1 cm. short of the mark on the needle. The stylet is removed and aspiration is used to determine whether or not the fluid is obtained. If none is obtained, the needle is advanced 5 mm., and the procedure is repeated. If still no fluid is obtained, the needle is pushed to the mark and a third attempt is made; and if here there is no fluid obtained, the needle is withdrawn, measurements are made again and another attempt is made. If the second attempt results in no fluid, the effort is discontinued, as, by this time, there is a possibility of hemorrhage.

In 200 patients in which cistern puncture was performed in this manner, one patient complained of giddiness and headache the following day, and another patient had slight meningeal signs and remained in bed for one day.

Comment

(1) In clinical practice, the depth of the cistern (DC) can be calculated from its rela-

tion with the flexion axis of the head. DC= DF−8 mm. + or −5 mm. The posterior mastoid point has the advantage of being in the same horizontal plane as the cistern, and thereby avoiding errors due to the variable heights of the tips of the mastoid process.

(2) The point of the insertion and direction of the needle must be such that the needle follows the shortest possible course to the cistern. The head must be in hyperflexion to insure maximal tension of the dura, when it is pierced by the needle.

(3) Cistern puncture is performed more easily in the upright posture, although this requires aspiration of the fluid. In the lateral decubitus there is free flow of fluid and somewhat less danger of acute cistern block. While the experienced physician does not always need the exact measurements, they are useful in learning the technique.

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A Family Manifesting Heredofamilial Spastic Paralysis

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It is difficult to formulate a definitive and final classification of all the degenerative diseases of the nervous system. These diseases are found in almost infinite variety and siblings affected with the same disease will often show varying clinical pictures. Abortive forms, so called "formes fruste," further confuse attempts at accurate classification. Nevertheless, careful observers, such as Sacks, Page, Schilder, Westfall, Friedreich, Wilson and others, have delineated certain classical disease entities which act as a guide for those of us who observe these rare entities today.

During the years we have seen many such clinical syndromes; Friedreich's disease, amaurotic family idiocy, peroneal muscular atrophy, Thomsen's disease, amyotonia congenita, etc. But this was our first experience with hereditary spastic paralysis, either through personal observation or through demonstration at many meetings which we attended.

The first case of family spastic paralysis was described by Strümpell in 1886. Rhein, in 1916, made a complete survey of this entity and summarized all the cases to that date. Paskind and Stone documented more cases and summarized the literature up to 1933. As of the present about 150 cases have appeared in the literature. According to Ford, males and females are equally affected.

On April 6, 1949, Mrs. S. brought her 12 year old son in for neurological study. The presenting complaint was "dragging of the legs." The history revealed that at 5 years of age this youngster began to complain of pain in both knees. He was examined and thought to be suffering from some type of rheumatism at the time. However, difficulty with his gait continued to progress and, at 8 years of age, he was studied at a hospital in Pittsburgh and confined thereafter to a home for crippled children for about two years. His gait difficulty continued to progress. His social and school adjustment were seriously interfered with on this account.

The examination revealed a thin white boy who walked with a peculiar, waddling gait, showing some spasticity in both lower ex-

tremities. Weakness seemed most marked in the region of the hip muscles. The patellar and Achilles reflexes were markedly hyperactive bilaterally and there was bilateral Babinski, Chaddock, Oppenheim and Rossolimo. The superficial and deep abdominal reflexes were weak and easily exhausted. There was a first degree horizontal nystagmus to either side, well sustained. Objective examination was otherwise negative and spinal fluid studies were normal in every respect.

Further probing into the history revealed that there was a sister and a brother who also presented some disturbance in gait. The sister, 10 years old, began to complain of fatigability on walking when she was about 6 years old. The mother further stated that she was prone to stumble and fall on the least provocation. The mother said that she seemed to be having somewhat more difficulty walking as time went on. On examination the young girl showed findings almost identical with those of her older brother. There was a spastic weakness of both lower limbs, the deep muscle reflexes were all hyperactive in the lower extremities and there was bilateral Babinski, Chaddock and Oppenheim.

There was a third youngster, a boy aged 5, whom the mother considered as "being normal." However, when brought in for examination this youngster, too, showed spastic weakness of both lower limbs, bilateral ankle clonus and bilateral Babinski.

The birth history and the early developmental history in all these children was considered normal.

When questioned about any familial tendency toward a similar illness, the mother stated that no member in the immediate family, whom she could recall, suffered from such an illness. However, it was noted that the mother, herself, walked with a waddling gait, suggestively similar to that of the older boy. We, therefore, decided to examine her and it was found that she, too, presented mild motor weakness in both lower extremities, absent abdominal reflexes, hyperactive deep muscle reflexes in both lower extremities and bilateral Babinski response.

Thus we had here a family consisting of a mother and three children, all afflicted with a neurological syndrome which affected chiefly the cortico spinal tract. It seemed to us that hereditary spastic paraplegia was the most probable diagnosis. It should be mentioned that most cases show some involvement of columns of Goll and Burdach and occasionally even cerebellar tract involvement in addition to pyramidal tract involvement.

The pathogenesis of this group of illnesses is conjectural. Gowers postulated that there is an inherent lack of vitality in certain portions of the nervous tissue. It was his opinion that this explained why specific areas of the nervous system begin to show early deterioration. He termed this group of diseases abiotrophies. Since the disease is both familial and hereditary, transmission in the germ plasm must be postulated.

Since we are as yet ignorant of any specific measures which may help to correct the inherited weakness of the nervous tissue, treatment must, of necessity, be symptomatic. In the present instance we recommended high vitamin diet including Vitamin E. We also suggested physio-therapeutic measures in an attempt to improve function in the involved muscles.

Summary

A family consisting of mother and three children, all presented evidence of spastic paraparesis. The clinical picture was that of heredo-familial spastic paralysis. This illness falls into the group of diseases which, at our present state of knowledge, are termed abiotrophies. Pathogenesis is not fully understood and treatment is therefore symptomatic.

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Flexibility and Experimentation in Psychotherapy

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It may add to the convenience of the therapist to find a single method of psychotherapy which can be applied generally to all patients in all situations but this is not the purpose of therapy. More important is it to add to the security and comfort of the patient. A number of years ago I had the opportunity of observing several people with anxiety reactions who recovered in the hands of a psychotherapist. These patients were free to talk to me and repeatedly they made such statements as this: "I am getting well but I haven't the slightest idea what he is talking about. I don't know the meaning of the words he uses." It became clear that healing was taking place in the realm of the feelings, and that perhaps we should not take our techniques in the intellectual sense too seriously; that more than one "technique" will get us to the same goal.

It was not difficult to see that patients were people with feelings but haven't we far to go in understanding our own emotional reactions and behavior in interviews? Many community clinics, in their training programs, are following the practice of transcribing and studying, not only what the patient said but also what the therapist said and how he felt about it.

Not long ago, in attempting to demonstrate negativism in a seventeen year old catatonic lad before a small class, I pulled the old grandstand stunt of telling him to keep his eyes closed tightly expecting that he would open them. It didn't work. I turned quickly and said: "After all, that was a poor attitude to take toward you. Let's change it." And then, with real regard, added: "I wonder if you wouldn't *like* to open your eyes and talk things over with us?" Thereupon, he not only opened his eyes but sat up, talked freely and was reluctant to terminate the interview when the time came. Too often we doctors have thought we had to be right, too often we conceal our errors. Can't we make better use of them? Patients will always forgive our technical errors—it may even be reassuring to know that we too, are human—but they can never forgive persistent and uncorrected sins of attitude.

Carl Whittaker has suggested as an additional check on the awareness of our own emotional reactions that we have another therapist present in the interview for the purpose of observing both. Harold N. Rosen recently tied up all of his psychiatric textbooks in a neat package, threw them in the river and went to work in earnest on some chronic schizophrenic patients with rather remarkable results. I believe this work is more important than we realize and that some of the priceless ingredients in his psychotherapy are his blind acceptance of patient's thinking and needs as reasonable and normal, his complete lack of hostility towards them, and sufficient security on his part so that he could give affection with absolutely no expectation of return. The vulgar language is probably important because of the strictness of parental attitudes on such matters. Moreover, he was able to use it as a vehicle for transference and for the expression of his complete acceptance of the patient.

Much can be learned by consulting the patient directly as to his needs. A young man, asked what qualities in the therapist he thought would be helpful in treatment, replied promptly, "Most of all, I don't want you to be professorial, stand-offish, authoritarian and please, don't be passive because my wife is so much that way, and don't tell me to figure out everything for myself, I need more than that." This is only one example of learning directly from patients. Too long have we been dominated by the carefully concealed feeling that our patients, by comparison with ourselves, don't know anything at all. Alcoholics have shown some skills in dealing with each other which have certainly not been our contribution. Possibly another anonymous organization would be in order for schizophrenics.

Emotional reactions can best be observed and dealt with under natural circumstances. Sometimes the "therapeutic hour" has be-

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come so sacred as to be stilted. Even telephone interruptions can be put to good use and they certainly can be a basis for discussion of the patient's feelings toward therapy and the therapist. Recently, a proud business man had just deflated his ego considerably by placing the marital cards on the table face up. He appeared much crestfallen when, at the crucial moment, the telephone rang and I spoke to an unexpected visitor from out of town who needed a hotel room. Could the patient help me? He jumped at the opportunity. He picked up the other phone, called a hotel manager and arranged for the room. He went away feeling better. He had done something for me.

On another occasion, while interviewing a young lady who was having difficulty getting into her childhood memories, I received a call from a patient. This time it was about a seven year old boy. He had four siblings, ranging in age from twenty-three to thirty-one. We discussed generally the case that caused the interruption and then she let go: "It wasn't that way with me. I was the oldest of eight and took care of all the rest. I grew up not wanting children. I worked hard and am just now realizing how much I have resented it." If another patient calls, he is quite likely to have many of the same problems as the one sitting in the office and much can be said over the telephone intended for both and it may be more effective than when directed to the person in the chair. It may be discussed by asking the patient later what he thought of the conversation.

Similarly, our records have always been regarded as strictly confidential. With a full recognition of the importance of the confidences placed in us, may we not sometimes overdo the regard for secrecy that we believe is imposed on us? Is it not possible that we could be fostering the very fear of shame and disgrace which we would like to dispel from the public mind? Margaret Mead, in a discussion at the 1948 American Orthopsychiatric Meeting, mentioned that the anthropologists, under field conditions, had had to learn to write of the behavior of people in terms that were acceptable to the observed as well as the observer.

Recently, a patient attempted to pick a quarrel with me. She had many hostilities at the start of an interview, and, among other things, was annoyed over the record that was being made. After a few minutes I was called from the room. Rather than be possessive of the record by taking it along or expose her to the temptation of reading it in my absence, I handed it to her to read and asked her to let me know if it was a fair report of our interview. It was mostly about sex and was considerate of her, and of course, was perfectly safe. This maneuver cleared the atmosphere and she was able to direct her hostilities again toward their real objects.

In regard to the number of people present at a treatment, we have ardent advocates of individual therapy and many who work with "the group." Is there not a place for joint discussions with two or three patients, a sort of family conference? This method has been especially useful where marital problems are in the foreground, and also, it seems to help with adolescents and their parents. Often, it may serve to clear away questions of partiality. At these sessions the therapist is put on his mettle for he must demonstrate his objectivity and neutrality and not just talk convincingly. If he is really impartial the discussions can be helpful.

It is sometimes of advantage to see several people together at the beginning of therapy in order to obtain mutual agreement on the broad outlines of their problems and to discuss the objectives of treatment. A reliable guide in selection of patients to form this group is to observe the spontaneity, enthusiasm and eagerness to help and to be included in the plan. If the problems are close to the surface this method is more useful and this fact usually can be ascertained before they appear for the meeting. Also the patient may be consulted directly about the desirability of including others and if agreeable, who might be invited and when would be the best time. Where the therapist is handling two people in the same situation, confidence may be renewed at crucial points where common decisions are made. During the interview it is important that conversations develop between only two of the three or more present. This situation may be met tions not develop between only two of the three or more present. This situation may be met directly by the simple reminder that this

is not the purpose of the meeting and such exchange of thoughts can be reserved for other occasions.

Among the ways in which we may find short cuts in psychotherapy, three approaches are worthy of special mention:

First, quicker realization of our own feelings, more immediate and direct management of our own hostilities. Love on a broader scale, involving many people, has to be developed, not in the sense of sentiment but in the sense of more complete acceptance. We have to learn not only to tolerate, but to work through annoying and frustrating habits which are almost always taken out on us.

Second, discerning and management of a pattern of behavior in only one relationship, for example, with the wife, even though this same habitual method of dealing with another person was learned early in life and, indeed, permeates all relationships. It may be that other connections need only be reviewed, not explored thoroughly. The most immediate and dramatic relationship should be selected.

Third, deliberate encouragement of, or actual projection of the life-problems or pattern of behavior on the intake situation and on the therapist. Psychiatric social workers have been particularly adept at pointing out the relationship between the problems of intake and the whole problem, the former often being a recapitulation of the latter. This is a variation of the second method and has been given special emphasis by the group at the Philadelphia Child Guidance Clinic. It has some advantages over the second, particularly in that both parties are available and secondary misunderstandings in reporting are obviated.

The constant influx of new material and new ideas from other fields into the therapeutic situation serves to keep it vitalized. We should read and listen to less of our own "stuff" and more of others. Otherwise, the therapist is likely to become bored and, therefore, to be boring to the patient who finds all of this difficult enough anyhow. For example, anthropologists have found that there is no significant homosexual problem in some societies where these biological deviations are regarded by people in general as of no importance. This can be turned into a new source of reassurance and face-saving for the person with homosexual conflicts. The finding that strabismus in another society may be regarded as sexually attractive, is a good means of de-emphasizing so-called physical inferiorities in general. The fact that eating together in another society may be attended by the same secrecy and feelings of shame as sexual activities are in our own gives new flexibility to the management of these feelings in people laden with guilt. They can see that this is only one way of looking at it.

We get into too many ruts. We develop pat labels like passive dependency and immaturity. We get the idea that everyone must be made to stand on his own feet and make decisions. We forget about too active and too early independence, forced independence and over-maturity that is like fruit ripened too soon. We talk glibly of permissiveness as though this solved all problems. We need to be permissive sometimes, restrictive, firm and even prohibitive at others. We must be directive this minute, permissive the next. We must have indulgence in our left hand, discipline in the right. Listening is not a religion but only a very good way to handle some situations.

We must beware of being resistant to simplification in psychotherapy lest our bag of tricks become understandable to others and, therefore, capable of wide diffusion. Complete acceptance of behavior, no matter how bizarre, as expressing normal needs, a management of our own hostilities and frustrations, surmounting of the culturally deeply-implanted ideas of disgrace permeating all mental and emotional problems, deeper faith in the reality of patient's pains and other complaints, the honest facing and utilization of our own mistakes, the willingness to unbend from our stiff professional pedestals, the ability to learn from varied sources including our patients, learning to express our feelings in terms acceptable to everybody, the refusal to worship any one method of procedure,—these are some of our really basic techniques.

Neurological Clinical Pathological Conference

OF THE CINCINNATI GENERAL HOSPITAL

CHARLES D. ARING, M.D., Editor

CASE NO. 250572

Presentation

A 36 year old white housewife was admitted to the hospital on May 9, 1949 because of severe respiratory distress. The patient had enjoyed good health until October 1945 when she first noted the occurrence of diplopia. This became apparent periodically whenever she used her eyes for reading or at the movies. Shortly thereafter she became conscious of a nasal twang to her voice for which she was treated unsuccessfully. Later she noted drooping of her eyelids and her lower jaw, and her husband observed that her eyes remained open when she slept. These symptoms progressed slowly until February 1946 when, because of weakness, she collapsed in the street and had to be carried to her home. A physician administered prostigmine and within "11 minutes" the patient was entirely relieved of her weakness. Since this episode the patient continued to take increasing amounts of prostigmine orally with benefit. Later, because of increased weakness, she had taken as many as 20 to 30 tablets in a single day. On this regimen she was able to carry out her housework adequately although she eliminated all unnecessary and heavy exertion.

In February 1949, while she was in Florida, her mother died unexpectedly in Cincinnati. On the way to the airport en route home the patient became very dyspneic and had to be placed in a respirator for 72 hours. This attack was associated with severe cyanosis and syncope. She later made the trip, completed her affairs and returned to Florida without mishap, but on April 1 she suffered another spell and had to be paced in a respirator. On this occasion and in many subsequent episodes it was noted that the attack was precipitated by an emotional disturbance, a temper tantrum and that, although unable to breathe she flailed about actively and shouted incessantly for help or in anger. On May 9 against her will she accompanied her husband upon a visit to some of his relatives and again suffered an attack of profound weakness and dyspnea. She was brought to the hospital in distress and became so distraught when her husband was not permitted to remain with her that she collapsed, became deeply cyanotic, ceased to breathe and lost consciousness. Deep reflexes disappeared and no intercostal muscle activity could be detected. Prompt introduction into the respirator brought about immediate relief. Later a psychiatric interview precipitated another attack which appeared to be relieved by a hypodermic injection of sterile water. Shortly afterward another severe attack occurred and she lapsed into unconsciousness until replaced in the respirator.

The patient was obviously of a brittle emotional nature and reacted violently when her whims were obstructed. She had been married twice, the first venture terminating in divorce. She had had 3 induced abortions in wedlock. Her career had been varied. She left medical school after failing the second year, became a graduate nurse and worked intermittently as a nurse, a laboratory technician and an office secretary. Both her present and her first husband were alcoholic, the latter having made a recent attempt at suicide. Her record showed a past history of hemorrhagic nephritis at 4 years, rheumatic fever at 8 years, double pneumonia at 13 years and catarrhal jaundice at 25 years. She claimed to have gone from 187 to 130 pounds during the past year.

Despite the history of weight loss and weakness the patient was well developed and nourished. She appeared well at the time of examination but continually rolled her eyes upward, wrung her hands and perspired profusely. Her gait was normal and her voice not remarkable. Pupillary activity was normal and ocular movements, though usually conjugate, occasionally showed a bilateral divergent squint. There were frequent tic-like movements of either eye which twitched in

varying directions. The upper and lower lids could not be completely approximated. The eyegrounds were normal. Tongue and facial movements were normal.

The thorax was symmetrical and normal motility was evident. There was no evidence of muscular wasting. The lungs were clear. Respirations were 20 per minute. The heart was normal. Temperature was 98.6 degrees F., pulse 80 per minute; blood pressure 105/65. Examinations of the abdomen and internal genitalia were normal. The anal sphincter had poor tone and was relaxed but the rectum was normal. The extremities showed no atrophy and though meticulous muscle testing was not carried out it was observed that the knee jerk was continued after 60 tappings. Deep reflexes were all within normal limits and no abnormal signs were elicited. There was weakness of the orbicularis oculi.

Red cells of the blood numbered 5 million with 13 grams of hemoglobin. The white cell count was 10,100 with 68 per cent neutrophils. The admission urine sample showed 3 plus glucose and 3 plus albumin. There was no abnormal sediment, no acetone and later samples were all normal. A Kahn test of the blood was negative as were the usual tests for liver function. The blood urea nitrogen was 11 mg. per cent, the fasting blood sugar was 100 mg. per cent, the CO_2 combining power was 46 volumes per cent, and the blood cholesterol was 125 mg. per cent. A glucose tolerance test showed no spilling and a range from 60 to 165 mg. per cent in 2 hours. A 24 hour urine sample was examined and found to contain 0.7 grams of creatine and 0.13 grams creatine per liter. A week later these figures were 0.95 grams and 0.12 grams respectively. (The record stated that these figures were well out of line with any anticipated values but that the presence of creatine was considered significant). A lumbar puncture was normal except for a protein content of 67 mg. per cent; sugar was 55 mg. per cent and the chloride, 747 mg. per cent. The gold curve and Wassermann tests were negative. An electroencephalogram was said to be abnormal and the basal metabolic rate elevated, but no definitive data were included. One electrocardiogram revealed a rate of 76; PR - 0.12; QRS - 0.08; T_1 flat and TV_1, V_2 and V_3 abnormal. Another showed a pulse of 114; PR - 0.16; QRS - 0.06 and T waves of low amplitude. A roentgen film of the skull and PA and lateral teleoroentgenograms were normal.

Under minor stress several emotional attacks were precipitated and though the respirator was required for apnea on some occasions, placebos were successful on others. The presence of a history of the ingestion of large amounts of the bromide salt of prostigmine, triple bromide solution and the presence of an acneiform eruption on the back excited interest which waned when the blood bromide content was not found to be excessive.

On May 19 a severe attack of breathlessness and anxiety was treated unsuccessfully with placebos for 3 hours and completely relieved within 20 minutes after the administration of prostigmine. Thereafter she was maintained on this drug and given additional amounts for each attack, always with benefit. On May 31 the patient was permitted to return to her home where she received 1 cc. of prostigmine by hypodermic injection daily.

The patient returned to the hospital at midnight on June 7. She had remained relatively free of symptoms until 7 p. m. on that evening when her husband accidentally broke the syringe before administering her evening medication. The patient became disturbed, severe breathlessness occurred and the Life Saving Squad was called. An ampule of prostigmine was given at 8 p. m. and another at 9 p. m. but the dyspnea and cyanosis continued in spite of vigorous artificial respiration.

At the time of entry her respirations varied from normal to flurries of shallow labored tachypnea. She jerked her extremities about in weird fashion, rolled her eyes and often propped her chin up with her hands. During the episode cyanosis was profound. Several more doses of prostigmine given subcutaneously and intravenously afforded only slight relief and she was placed in a respirator. When she was removed from the apparatus on the following day she appeared to be in a frenzied state. Although not cyanotic she repeatedly asked for help, prostigmine or artificial respiration. At 6 p. m. her apprehension seemed so great that she was again placed in a respirator. While this was being affected she was given manual artificial respirations, oxygen by mask and both prostig-

mine and adrenalin intravenously. However, cyanosis deepened, spontaneous respirations and other muscular movements ceased, she became unconscious and died at 7:15 p. m. A weak apical cardiac beat could be detected until shortly before death.

Clinical Discussion

Dr. Charles D. Aring: I saw this patient on one occasion on the ward during her next to the last admission and my diagnosis was myasthenia gravis. Since I find nothing in the protocol to dissuade me from this opinion, I thought I would discuss myasthenia gravis, directing my remarks particularly to the students.

Myasthenia gravis is a syndrome whose main signs are fatigue, weakness and at times wasting of muscles, chiefly those supplied by cranial nerves. It has a variable pathology, lesions have been found in muscles, endocrine glands and other tissues though none of them are constant.

The incidence is the same in the sexes although the disorder usually appears a decade earlier in the female. The extremes of age of onset have been reported as 8 and 71 years. The third decade is the period of greatest liability. Familial instance while known is rare.

The onset is generally insidious. If patients are seen during the period of their initial symptom or symptoms, a correct diagnosis is unusual. The most frequent onset is with tiredness or weakness of a portion of a muscle, a muscle, or muscles supplied by a motor cranial nerve(s), a not unusual onset in multiple sclerosis. At times similar muscle symptoms begin in the limbs. Generalized weakness is another first symptom. The motor functions bear the brunt, though pains and aches sometimes occur.

The pathognomonic sign of the disorder is the induction of fatigue by repetitive movement, milder cases do not exhibit their defects until evening. Just as important is the restoration of function by rest. Although weakness is at times relatively restricted, muscles showing good power to begin with are often incapable of sustained contraction. Activity of one set of muscles may tire others. Experimentally the exercise of an arm of a myasthenic patient with a tourniquet applied, may result in weakness of distant musculature when the tourniquet is released.

A night's sleep usually improves the myasthenic patient and debility returns in the course of the next day. The patient becomes tired with the ordinary movements of living, without having to exercise a part violently or repetitively. In some cases repeated tapping of the quadriceps tendon will abolish the knee jerk, somewhat as repeated light stimulation may abolish the pupillary reflex.

In advanced cases paralysis is often complete in certain muscles innervated by motor cranial nerves. Wasting occurs in about 10 per cent of cases most often in those muscles innervated by the fifth and seventh cranial nerves and those of the shoulder girdle.

The myasthenic face is common; ptosis is frequent as are various ocular palsies. The facial features are smooth. As the result of paralysis of zygomatic and risorius muscles while the levators of the upper lip are spared, there results on attempting smiling a snarl rather than a smile. Weak laryngeal muscles, and easy fatiguability of intercostals, diaphragm and sternocleidomastoids, result in attacks of dyspnea often alarming and sometimes fatal, lasting from minutes to hours, they develop seemingly spontaneously or on moderate exertion.

Typically there is descending involvement of muscles supplied by motor cranial nerves (III, IV, VI, V, VII, IX, X, XI, XII), they may of course be affected simultaneously. There follows involvement of trunk and limb muscles, but paretic selection and extension may be irregular. A few cases start in or effect primarily muscles of neck, trunk and proximal limb; sometimes on standing the knees give way first.

Early in the disease symptoms are prone to come and go, and remissions are not infrequent; later most of the abnormalities become fixed. A steadily progressive course is not unusual. Acute forms may bring death within a year of onset but duration of 20 or more years is known. Relapses are typical even as much as remissions. Attacks of dyspnea are common, and death in them is not infrequently quite unexpected.

The response to neostigmine, an analogue of physostigmine is diagnostic. In 1934 Mary Walker,[6] reasoning that the disorder resembled curare poisoning, applied the antidote physostigmine thereby discovering our

most potent therapeutic agent up to now.[7] The response of myasthenia gravis to neostigmine is unlike that of any other condition. Perhaps as important diagnostically is the fact that neostigmine in the doses ordinarily employed in treating myasthenia gravis, sets up fasciculations in muscles of normal persons and in all cases of muscular disease except myasthenia.[3] The twitchings though generalized are most readily observed in the eyelids and tongue.

The cause of the disease is not known. Torda and Harold Wolff[5] have determined that the immediate cause of the symptoms of myasthenia gravis is a decrease in acetylcholine synthesis. At the June 1949 meetings of the American Neurological Association they reported that they induced incomplete remission in five moderately to severely ill patients by the administration of a total of 400 mg. adrenocorticotrophic hormone, using 20 mg. every six hours. They used this hormone because it increases acetylcholine in vivo. Other reasons for using this substance were as follows: it is generally known that increased lymphatic tissue (lymphorrhages) and "hyperfunctioning" thymus have been found in myasthenia gravis. Tissue fractionation studies have shown that one of the sources of the substances that inhibit acetychloline synthesis is the thymus. Administration of adrenocorticotrophic hormone induces reduction in the mass of the thymus and the lymphatic tissue. Removal of the pituitary gland in rats induces changes in the electromyogram that closely resemble abnormalities noted in patients with myasthenia gravis. And finally some patients dying with myasthenia gravis have had an accumulation of an eosinophilic colloid material in the pituitary gland, suggesting altered function of the gland.

A few points in the laboratory diagnosis in our case. Patients with muscle atrophy or muscle dystrophy show a raised creatinuria which increases with increased protein intake. Unlike normal adults they eliminate a large amount of ingested creatine, rather in proportion to the severity of the disease.

Creatinuria is present in infants and young children, in females during menstruation, lactation and after delivery, in acute fevers, acidosis, starvation, excessively high protein diet, low carbohydrate diet, and disturbed endocrine function. The greater the incapacity of the patient the smaller the amount of creatinine excretion, the normal adult male excretes about 1.5 grams in 24 hours which varies with exercise, metabolic rate and diet.

Since the histopathology of myasthenia gravis is notoriously inconstant it is risky to try to predict the abnormalities that Dr. Gall will describe in our case. Perhaps the commonest change is the deposition of masses of small round cells, indistinguishable from lymphocytes, in myasthenic muscles. For a half-century these have been known as lymphorrhages. They may be found in other viscera—heart, liver, lungs, endocrines, etc. They have been rather generalized throughout the tissue in some cases, and completely absent to thorough search in others. They bear no relationships to length or severity of the disorder. Myasthenic muscles may undergo all sorts of degenerative or atrophic changes.

A common lesion is a persistent and enlarged thymus gland, said to be present in 50 per cent of cases. This may be part of a more widespread process, e.g. status lymphaticus. The thymus abnormality has been diagnosed most often as benign thymoma, all gradations of tumor including thymic carcinoma have been found in myasthenia gravis. The volume and consistency of the thymoma vary considerably from case to case.

Careful search of the nervous system, central and peripheral, usually has been unrewarding; perivascular accumulation of epitheloid and lymphocytic cells within the nervous system is unusual.

There would appear to be little doubt as to the diagnosis of myasthenia gravis in this case. Whether or not there was a thymoma is guesswork now. It was not percussed in the multiple physical examinations that the patient should have had, and though I find the results of all sorts of laboratory examinations, there is no mention of roentgen examination of the chest. There was a teleoroentgenogram which I take to mean concentration on the heart. Perhaps there is in reserve a chest plate to be presented here.

The predominance of respiratory signs makes me suspect that she had a thymoma and even a large one, perhaps encroaching

on the anterior mediastinum. As I recall my single visit to this patient, I mentioned the incidence of thymoma in myasthenia gravis but, if my recollection is correct, the physicians gathered round were somewhat skeptical of this diagnosis and were more interested in pointing to her angular personality. I prefer to leave that complex part of the story since I'm afraid Dr. Gall can't help us much in this area. Though I believe it of vital importance, this doesn't happen to be the place to discuss the emotions. I don't want to close without saying what has been repeated over and over by many teachers in this institution; placebos have been successful in relieving physical symptoms and signs[1,4] of advanced carcinoma, angina pectoris,[2] bronchiolar spasm and of many another disease. When a doctor administers a medicine to a patient and particularly when he does the actual work of administration himself, he gives the patient more than that contained in a syringe, capsule or teaspoon.

Clinical Discussion

Dr. M. A. Blankenhorn: May we have a reading of the x-ray films?

Dr. Donald K. Bailey: I must correct the report on the protocol. The film was read as "negative" by one of the residents but shortly thereafter was reviewed and a mass was readily discerned in the anterior superior mediastinum. I would judge from its contours that it measured approximately 4.0 cm. in diameter and it was located in the supracardiac region, probably anterior to and in contiguity with the parietal pericardium sheathing the great vessels. The shadow is homogeneous, shows no evidence of calcification and is consistent with a thymoma. Neither "plunging thyroid" nor tuberculous lymph nodes seem likely.

Unfortunately this corrected report of the film failed to reach the record to supplement the original reading.

Dr. Aring: It would not have altered my opinion. The disease was obviously myasthenia gravis and the presence of a mediastinal mass would simply lend further weight to the evidence at hand.

Dr. Albert A. Brust: It may be of some interest to report that this patient had had many roentgen studies of her chest outside of this hospital and in none was a mass reported. Incidentally, she had a therapeutic trial of deep radiotherapy over the upper sternal region and no beneficial effects were noted.

Dr. Blankenhorn: Was the mass of such size or location that it could have caused respiratory symptoms?

Dr. Bailey: No. It was situated anteriorly and was not in relation to either the trachea or bronchi. Nor would its size have permitted critical space consumption.

Dr. Aring: I think there was adequate disturbance of muscular function to account for the dyspnea without attempting to incriminate the thymic tumor, if that is what the mass is.

Dr. Bailey: I should like to add that fluoroscopic study is often a better means of detecting such lesions than the postero-anterior roentgenogram.

Pathological Discussion

Dr. Edward A. Gall: Necropsy was carried out 4 hours after death. The body was both well developed and nourished and no evidence of muscle wasting or atrophy was encountered. Indeed, the salient gross findings were few. Save for a thymic mass in the superior mediastinum no other gross abnormalities were detected.

The mediastinal tumor was lobulated, thinly encapsulated and separably adherent to the adjacent pericardium. It measured 4 x 3 x 2 cm. and on section had a mottled reddish yellow appearance containing several cleft like cystic spaces. The remaining viscera were not remarkable, the thyroid being normal in size and conformation and the lymphoid tissue having normal bulk and distribution.

Microscopic studies were somewhat more revealing. There were 10 sections of skeletal muscle and in 2 of them there were small, but dense, interstitial clusters of lymphocytes consistent with the so-called "lymphorrhages" which are recognized so commonly in association with myasthenia gravis. The muscle fibers were otherwise entirely intact. The spotty occurrence is a widely recognized characteristic and it is of interest that the lymphorrhagic phenomenon does not appear in relation to the muscle weakness[8] but seems to show no predictable distribution.

The heart muscle showed none of these

foci but there was a striking interstitial edema which was frankly pathologic in nature. I have no idea of its significance although I suspect it was a result of the severe anoxia from which the patient suffered. The circumstance of myocardial alteration in myasthenia gravis, though not unique, is an unusual finding.[9] The brain, also, was the seat of multiple areas of anoxic cortical degeneration of relatively recent origin. There were foci of nerve cell degeneration and hemorrhage but little reactive inflammation and no gliosis. These lesions were attributable undoubtedly to the prolonged period of apnea and probably contributed in some measure to the ultimate failure to respond to therapy. The lungs showed, as the concluding event, a severe degree of pulmonary edema and evidence of early pneumonic consolidation.

Sections of the thymic tumor showed it to be composed of a uniformly distributed dense aggregation of lymphocytes intermingled with which were larger, palely staining elements variously termed "epithelial" or "epithelioid" cells. From their appearance one would suspect that they were actually of mesenchymal origin. The appearance of the process was entirely similar to the type of thymoma most commonly associated with myasthenia gravis.[10] Despite its resemblance to lymphoma the lesion is undoubtedly benign and, as a matter of fact, may well represent a hamartoma rather than a true neoplasm.

There are really no pathognomonic features of myasthenia gravis although the contribution of the clinical observations, the thymoma and the muscular lymphorrhages make this diagnosis reasonably certain. Most of the other muscular and nerve disorders with which this disease may be confused can be excluded by the absence of significant histologic alterations.

The association, or as some would have it, coincidence of a thymic lesion and myasthenia gravis was first recorded by the German pathologist, Weigert, in 1901. It is now generally appreciated that upwards of 30 per cent of the cases with this disease have a concomitant thymoma and another 10 to 20 per cent exhibit non-neoplastic thymic enlargement. In the latter group and in 75 per cent of the remainder without grossly perceptible abnormality of the organ, Castleman and Norris[11] have demonstrated the presence of lymphoid germinal centers, a change which is said not to occur with any degree of frequency except in myasthenia gravis. This follicular lesion was not apparent in the residual thymic tissue in the present case.

Clinical Diagnosis

Myasthenia gravis.

Dr. Aring's Diagnosis

Myasthenia gravis.

Pathological Diagnosis

Thymoma with myasthenia gravis.

Focal muscle lymphorrhage.

Focal cerebral degeneration and hemorrhage, anoxic.

Myocardial edema, severe.

Lobular pneumonia, early with pulmonary edema, severe.

Dr. William A. Ashe: Is it customary for the cyanosis to continue under treatment with adequate amounts of prostigmine?

Dr. Aring: That is probably not unusual in the more severe forms of the disease and especially in its terminal phase.

A Student: What bearing do you think the cerebral damage had on failure of response to therapy?

Dr. Gall: I don't know how one can say, although I suspect that it had some detrimental influence.

Dr. Brust: In one series of 33 cases with myasthenia gravis 9 patients showed changes in the electrocardiograms. These were tachycardia, T wave alteration or depressed ST segments. There was reversion to normal tracings with proper therapy.

Dr. Blankenhorn: Dr. Aring, what diagnostic value is there in the effectiveness of prostigmine in producing muscle fasciculation?

Dr. Aring: This is of importance in the diagnostic use of prostigmine. Muscle fasciculation occurs with the parenteral use of prostigmine or neostigmine in the normal, in other words in the person who does not have myasthenia gravis. A peculiarity of the myasthenic muscle is that it does not readily fasciculate to the usual doses of neostigmine, although large doses of the drug may cause even some muscles of the myasthenic patient to fasciculate.

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